

# INTERNATIONAL SEARCH REPORT

International Application

PCT/US 91/00245

## I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all)

According to International Patent Classification (IPC) or to both National Classification and IPC

see attached sheet

## II. FIELDS SEARCHED

Minimum Documentation Searched \*

Classification System	Classification Symbols

see attached sheet

Documentation Searched other than Minimum Documentation  
to the Extent that such Documents are Included in the Fields Searched:

see attached sheet

## III. DOCUMENTS CONSIDERED TO BE RELEVANT \*\*

Category \*      Citation of Document, if with indication, where appropriate, of the relevant passages \*\*\*      Relevant to Claim No. \*\*

see attached sheet

- \* Special categories of cited documents: 13
- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "Z" document member of the same patent family

## IV. CERTIFICATION

Date of the Actual Completion of the International Search:

14 MARCH 1991

Date of Mailing of this International Search Report:

26 APR 1991

International Searching Authority:

ISA/US

Signature of Authorized Officer \*\*

*Garrison E. Bugajski*  
GARRISON E. BUGAJSKI

PCT/US/ 91/00245

Attachment to Form PCT/ISA/210

I. Classification of subject matter

IPC(5): C12P 21/06; C12N 15/00

U.S. Cl.: 435/69.1, 172.3; 800/2

II. Fields searched

U.S. Cl. 435/69.1, 69.6, 70.1, 172.3; 436/547; 530/387; 800/2;  
935/22, 65, 106

Databases: Dialog Information Services Online (File sets Medline  
and World Patent Index)

Automated Patent System (File USPAT)

gene transfer or gene replacement or gene inactivation,  
homologous recombination; embryonic stem cell, animal stem cell,  
embryonal carcinoma, transgenic animal or mammal, xenogeneic  
antibody or antiserum or immune response, immunoglobulin;  
immunoglobulin gene.

Attachment to Telephone Memorandum  
PCT/US91/00245

Observations where unity of invention is lacking

Detailed reasons for holding lack of Unity of Invention.

There are three groups of claims: Group I is a method for producing antisera; transgenic animals; Group II is for embryonic stem cells. Group I is related as first mentioned product and process of use. Group III consists of a second mentioned product, which can exist independently of the first mentioned product. PCT Rules 13.1 and 13.2 do not provide for multiple products.

Itemized summary of claims groupings

I. Claims 1-7, drawn to a method for producing xenogeneic antisera, classified in Class 435, subclass 69.1.

Claims 8-18, drawn to transgenic animals with lesions in endogenous immunoglobulin genes, so that they can only express human immunoglobulin genes, classified in Class 800, subclass 2.

II. Claims 19-25, drawn to embryonic stem cells with lesions in endogenous immunoglobulin genes, classified in Class 435, subclass 230.1.

III. Documents considered relevant

<u>Category</u>	<u>Citation</u>	<u>Claims</u>
Y,P	US, A. 4,959,313 (TAKETO) 25 September, 1990 see entire document.	19-25
Y,P	US, A. 4,950,599 (BERTLING) 21 August, 1990 see entire document.	8-25
Y	Proc. Natl. Acad. Sci., USA. Vol. 83, issued April 1986, K.-I. Yamamura, et al., "Cell-type-specific and regulated expression of a human $\gamma 1$ heavy-chain immunoglobulin gene in transgenic mice", pages 2152-2156, see entire document.	1-25
Y	Proc. Natl. Acad. Sci., USA. Vol. 86, issued November 1989, B. Koller, et al., "Inactivating the $\delta 2$ -microglobulin gene in mouse embryonic stem cells by homologous recombination", pages 8932-8935, see entire document.	1-25
A	Proc. Natl. Acad. Sci., USA. Vol. 83, issued July 1986, D. Ayares, et al., "Sequence homology requirements for intermolecular recombination in mammalian cells", pages 5199-5203, see entire document.	8-25
A	Proc. Natl. Acad. Sci., USA. Vol. 85, issued February 1988, R. Brinster, et al., "Introns increase transcriptional efficiency in transgenic mice", pages 836-840, see entire document.	1-25
Y	Prog. Nucleic Acid Res. Mol. Biol., Vol 36, issued 1989, R. Kucherlapati, "Homologous recombination in mammalian somatic cells", pages 301-310, see entire document.	1-25
Y	Proc. Natl. Acad. Sci., USA. Vol. 86, issued October 1989, A. Shimizu, et al., "Immunoglobulin double-isotype expression by trans-mRNA in a human immunoglobulin transgenic mouse", pages 8020-8023, see entire document.	1-25